

PATENT APPLICATION

Our Docket No. 20020113.ORI

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re App : Fionula M. Brennan et al : March 3, 2008  
S.N. : 10/088,801 : Group Art Unit 1644  
Filed : September 18, 2002 : Examiner Zachary Skelding  
For : THERAPEUTIC METHODS AND COMPOUNDS

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**LETTER**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Suggested new claims indicated as allowable by the Examiner  
are attached for approval.

Respectfully submitted,

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132(new). A method of identifying a compound that selectively inhibits cytokine-stimulated T cell ( $T_{ck}$  cell) induced production of  $TNF\alpha$  by monocytes at least two-fold greater than the compound inhibits T cell antigen receptor-stimulated T cell ( $T_{tcr}$  cell) induced production of  $TNF\alpha$  a by monocytes

wherein said method comprises the following steps:

- (a) providing a population of  $T_{ck}$  cells wherein said  $T_{ck}$  cells have been produced by incubating normal human peripheral blood T cells with cytokines selected from the group consisting of:
  - (i) IL-15;
  - (ii) IL-6,  $TNF\alpha$  and IL-2; and
  - (iii) IL-6,  $TNF\alpha$  and IL-15;
- (b) providing a population of  $T_{tcr}$  cells wherein said  $T_{tcr}$  cells have been produced by incubating normal human peripheral blood T cells with one or more anti-T cell antigen receptor antibodies which activate T cell antigen receptors;
- (c) incubating separate cultures of  $T_{ck}$  cells and  $T_{tcr}$  cells with a compound to be tested;
- (d) resuspending the cultures of  $T_{ck}$  cells and  $T_{tcr}$  cells in the absence of the test compound;
- (e) fixing the cultures of  $T_{ck}$  cells and  $T_{tcr}$  cells;

(f) co-culturing equal portions of each of said fixed  $T_{ck}$  cells and  $T_{tcr}$  cells with monocytes to allow stimulation of the monocytes; and

(g) assaying for  $TNF\alpha$  production by said monocytes, wherein the method identifies a compound that selectively inhibits  $T_{ck}$  cell induced production of  $TNF\alpha$  by monocytes at least two-fold greater than the compound inhibits  $T_{tcr}$  cell induced production of  $TNF\alpha$  by monocytes.

133(new). A method according to claim 132 wherein said compound is an antibody having specificity for  $T_{ck}$  cells.

134(new). A method according to claim 132 wherein said compound has efficacy in the treatment of rheumatoid arthritis.

135(new). A method according to claim 132 wherein said anti-T cell antigen receptor antibody is an anti-CD3 antibody.